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EXAMINER	
PATEL, SUDHAKER B	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 08/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,015	BASHIARDES ET AL.	
	Examiner	Art Unit	
	Sudhaker B. Patel, D.Sc.Tech.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *1-14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/480,965.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/02 & 4/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' communication paper dated 4/9/04 is acknowledged. Claims 1,2 are related to pharmaceutical compositions of the generic Formula (I). Claims 3-5 are the compounds' claims, claims 6-13 are the process of making the compounds, and claim 14 is the method of use claim for the compounds of the Formula (I). Therefore, the claims in this application are the claims 1-14.

After further review and consideration, this application is found not ready for allowance for reasons stated bellow.

Specification

1. The disclosure is objected to because of the following informalities: The specification does not recite this application's relationship with the earlier U.S. Applications, as well as its relationship with other foreign applications.

Appropriate correction is required.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on 7/30/02 & 4/9/ are being considered by the examiner. Signed copy of the PTOP Form 1449 is enclosed with this communication for applicants' record.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA

1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims1-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6392042. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant pharmaceutical composition claims 1,2 are overlapping with ref.'042 claims 1,2(see column 16 lines 50-65, and columns 17-18). Instant compounds' claims 3-5 overlap with ref.'042 claim 3-5) see column18, lines 29-65 and columns 19-20. Instant process claims6-13 are overlapping with ref.'042 claims 6,7(see column 21 lines 1-5, and column 22 lines 1-6). Instant method of use claims overlaps with ref.' 042 claim 8(see column 22 lines 9-15).

5. The instant application differs from the ref.' 042 by reciting broader scope of compound and method of for these compounds recited in generic Formula (I). .

This will extend the monopoly of the ref.' 042.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 1-2 recite pharmaceutical compositions for the compounds of generic Formula (I) or its salt. Usually and inert carrier is also present in such compositions. Correction(s) is required.

9. Claims 1-2 does not recite amount of the compounds in a composition. Addition of: " therapeutically effective amount of compound of Formula (I)" is required.

10. Claims 1,3,14 recite Formula (II) twice. See lines 7 and 13. The structures represented by these 2 Formulae are different. Correction is required.

11. Process claims 6,8,1012 recite Formula (II). It is not very clear what is exactly claimed herein. Formula (II) of claims 1,3,14 have double meanings because they do not claim the same compounds.

12. Process claims 6-13 recite certain combination of the intermediates, but the claims do not recite the exact and definite nature of the end and FINAL compounds manufacture. What are exact chemical configurations of the compounds made?

13. Claim 14 recites the method for treatment or prevention of diabetes or complications of diabetes. What is included in prevention? What is also included in the terms "diabetes and complications of diabetes"?

14. The terms recited in 13. above will raise additional issues related to enablement as per 35 U.S.C. 112 paragraph one. See rejections bellow.

15. Claim 14 remains silent about the exact method of administration. Is the compound orally administered or by a patch?

16. Claim 14 does not recite the exact amount of the compound administered. Correction to:" therapeutically effective amount" is required.

17. Claim 14 recites "a patient". What is included by this recitation?

18. Claim5 recites compound and their salt. Correction to compound or their salt is required.

Claim Rejections - 35 USC § 112

19. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

20. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment OF A SINGLE, EXACT, AND SPECIFIC DISEASE, does not reasonably provide enablement for GENERIC DISEASES INCLUDED BY THE TERMS: DIABETES & COMPLICATION OF DIABETES". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Receptor binding is known to be structure sensitive. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. See also MPEP2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a), August 2000 edition, which are:

.***(1).*** The nature of invention;
(2). The state of prior art ;
(3). The predictability or lack thereof in the art;
(4). The amount of direction or guidance present;
(5). The presence or absence of working examples;
(6). The breadth of the claims, and
(7). The quantity of experimentation needed.

Following references are sited to show the sate of art(s).

- **Insulin resistance by art known compounds:**

Lebovitz et al(PubMed Abstract 11237217, also cited as Recent Prog. Horm. Res., 56,265-94(2001)) state that:" The exact mechanisms by which these agents decrease insulin resistance is not clear but they do decrease the elevated free fatty acid levels present in insulin-resistant patients and they appear to change the body distribution of adipose tissue".

- **Treatment possibility of hepercholestroaemia associated with hypertriglyceridaemia:**

Paragh et al(Pub Med Abstract 9406614, also cited as Acta Biol. Hung. 48/3, 359-67(1997)) state that:" The apolipoprotein A1..... increased significantly in during the second month of acipomox administration. The acid levels decreased in both groups, but significant change could be detected mainly in the NIDDM group."

Applicants' testing was done on animals, and not on the human beings at the time of filing this application on 7/17/1997.

Specification in pages 28-31 describes various tests and assays used for evaluation. The results of the protocol obtained are not presented for the actual compounds made and tested. The specification concludes the testing as:" In this test,

the compounds according to the invention exhibit a percentage of inhibition of glycaemia of greater than or equal to 10%". See page 29 lines 15-17.

Therefore, such assays and results will serve the purpose of preliminary screening of the compositions, which are of either single compounds or a combination of compound and its salts.

The facts as provided above do support the need for additional quantity of experimentation, which would be an undue burden to one skilled in the pharmaceutical arts, since there is inadequate guidance given to the skilled artisan, regarding the method of prevention for various disorders/diseases related to different body organs as well as different pathophysiology.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of instant compounds to control or prevent disorders related to inflammation

When the best efforts have failed to achieve a goal, it is reasonable for the PTO to require evidence that such a goal has been accomplished, *In re Ferens*, 163 USPQ 609. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006.

21. The abstract of the disclosure is objected to because it consists of 2 pages. Correction is required. See MPEP § 608.01(b).

Conclusion

Allowable Subject Matter

22. Claims 1-13 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph and other rejections, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

23. If applicants provide additional evidence to support the method of use claim for treating a single, exact and definite disease, the method of treating the same would also considered for allowance

24. The following is a statement of reasons for the indication of allowable subject matter: The closest prior art ref. Shigematsu et al(Chemical Abstract DN 90:19276, also cited as Jpn Tobacco and salt Public Corp., JPn Kokai Tokkyo Koho, JP 530 90401 dated 8/1978) teaches making and using of compounds with a core:" 1,2,3,5-Butanetetrol,1-[5-(2,3,4-trihydroxybutyl)pyrazinyl-:. See Compound with CAS RN # 68510-02-1.

25. The ref. '401 does not indicate or suggest to arriving at the instant invention.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhaker B. Patel, D.Sc.Tech. whose telephone number is (571) 272-0671.

The examiner can normally be reached on 6:30 to 5:00 pm (Monday-Thursday). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund J. Shah can be reached on (571) 272 0674 or Sr. Examiner Mr. Richard Raymond at (571) 272 0673 or Mr. James O. Wilson at (571) 272-0661.

The fax phone numbers for the organization where this application or proceeding is assigned are 703 308 4556 for regular communications and 703 308 4556 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1235.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sudhaker B. Patel, D.Sc. Tech.
August 23, 2004

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